

505  
1 1. A pharmaceutical composition, comprising a  
2 mixture of active compounds (A) a pharmaceutically active  
3 polypeptide, and (B) an enhancer compound which enhances the  
4 systemic absorption of said polypeptide in the lower  
5 respiratory tract of a patient, said mixture being in the  
6 form of a dry powder for inhalation, in which at least 50%  
7 of the total mass of active compounds consists of primary  
8 particles having a diameter less than or equal to about 10  
9 microns, said primary particles optionally being formed into  
10 agglomerates.

Sub A  
1 2. A pharmaceutical composition as claimed in claim  
2 1, additionally comprising a pharmaceutically acceptable  
3 carrier, which comprises either  
4 (a) particles having a diameter of less than about  
5 10 microns, such that at least 50 % of the resultant powder  
6 consists of optionally agglomerated primary particles having  
7 a diameter of less than about 10 microns; or  
8 (b) coarse particles, such that an ordered mixture  
9 is formed between the active compounds and the said carrier.

1 3. The composition of claim 1, wherein said  
2 polypeptide is a polypeptide hormone.

*Sub G2*  
1 4. The composition of claim 3, wherein said hormone  
2 is vasopressin, a vasopressin analogue, desmopressin,  
3 glucagon, corticotropin (ACTH), gonadotrophin (luteinizing  
4 hormone, or LHRH), calcitonin, C-peptide of insulin,  
5 parathyroid hormone (PTH), human growth hormone (hGH),  
6 growth hormone (HG), growth hormone releasing hormone  
7 (GHRH), oxytocin, corticotropin releasing hormone (CRH),  
8 somatostatin analogs, gonadotropin agonist analogs (GnRHa),  
9 atrial natriuretic peptide (hANP), thyroxine releasing  
10 hormone (TRHrh), follicle stimulating hormone (FSH), or  
11 prolactin.

1 5. The composition of claim 1, wherein said  
2 polypeptide is a growth factor, interleukin, polypeptide  
3 vaccine, enzyme, endorphin, glycoprotein, lipoprotein, or  
4 polypeptide involved in the blood coagulation cascade, that  
5 exerts its pharmacological effect systemically.

1 6. The composition of claim 1, wherein said  
2 polypeptide has a molecular weight of less than 30 kD.

1 7. The composition of claim 1, wherein said  
2 polypeptide has a molecular weight of less than 25 kD.

1 8. The composition of claim 1, wherein said  
2 polypeptide has a molecular weight of less than 20 kD.

1 9. The composition of claim 1, wherein said  
2 polypeptide has a molecular weight of less than 15 kD.

1 10. The composition of claim 1, wherein said  
2 polypeptide has a molecular weight of less than 10 kD.

1 11. The composition of claim 1, wherein said  
2 enhancer compound is a surfactant.

1 12. The composition of claim 11, wherein said  
2 surfactant is a bile salt, a bile salt derivative, an alkyl  
3 <sup>glycoside</sup> glycoside, a cyclodextrin or derivative thereof, or a  
4 phospholipid.

1 13. The composition of claim 11, wherein said  
2 surfactant is a salt of a fatty acid.

1 14. The composition of claim 11, wherein said fatty  
2 acid has 10-14 carbon atoms.

1 15. The composition of claim 14, wherein said fatty  
2 acid is capric acid.

1 16. The composition of claim 11, wherein said  
2 surfactant is sodium caprate.

1 17. An inhaler device containing the composition of  
2 claim 1.

1 18. The inhaler device of claim 17, wherein said  
2 composition is in the form of said agglomerates, said device  
3 being configured to induce the majority of said agglomerates  
4 to break down into particles having a diameter less than or  
5 equal to about 10 microns, upon inhalation of said  
6 agglomerates from said device.

1 19. The inhaler device of claim 17, which inhaler  
2 device is a unit dose, breath actuated, dry powder inhaler  
3 for single use.

1 20. The inhaler device of claim 17, which inhaler  
2 device is a multi dose, breath actuated, dry powder inhaler  
3 for multiple use.

1 21. A method for systemic administration of a  
2 pharmaceutically active polypeptide, comprising  
3 providing a composition comprising a mixture of  
4 active compounds (A) a pharmaceutically active polypeptide,  
5 and (B) an enhancer compound which enhances the systemic  
6 absorption of the polypeptide in the lower respiratory tract  
7 of a patient, said composition being in the form of a dry  
8 powder; and  
9 causing said patient to inhale said composition;  
10 provided that the diameter of the particles of the active  
11 compounds at the point they enter the respiratory tract of  
12 the patient is less than or equal to about 10 microns.

1 22. The method of claim 21, wherein said  
2 composition is inhaled from an inhaler device which contains  
3 said powder in the form of agglomerates of said particles,  
4 said agglomerates being substantially deagglomerated prior  
5 to entering the respiratory tract of said patient.

1           23. A process for the manufacture of a  
2 pharmaceutical composition suitable for administration by  
3 inhalation, comprising  
4           providing a solution in which are dissolved (a) a  
5 pharmaceutically active polypeptide, and (b) an enhancer  
6 compound which enhances the systemic absorption of the  
7 polypeptide in the lower respiratory tract of a patient;  
8           removing the solvent from said solution to yield a  
9 dry solid comprising said polypeptide and said enhancer  
10 compound; and  
11           pulverizing said dry solid to produce a powder.

1           24. A process for the preparation of a  
2 pharmaceutical composition suitable for administration by  
3 inhalation, comprising  
4           dry mixing (a) a pharmaceutically active  
5 polypeptide, and (b) an enhancer compound which enhances the  
6 absorption of the polypeptide in the lower respiratory tract  
7 of a patient; and  
8           micronizing the obtained mixture.

1           25. A process for the manufacture of a  
2 pharmaceutical composition suitable for administration by  
3 inhalation, comprising  
4           providing a first micronized preparation comprising  
5 a polypeptide and a second micronized preparation comprising  
6 an enhancer compound which enhances the absorption of the  
7 polypeptide in the lung of a patient; and  
8           mixing said first and second micronized  
9 preparations.

23

1 26. The method of claim 21 wherein the polypeptide  
2 is a polypeptide hormone.

*Subd. G3*  
1 27. The method of claim 26 wherein said hormone is  
2 vasopressin, a vasopressin analogue, desmopressin, glucagon,  
3 corticotropin (ACTH), gonadotrophin (luteinizing hormone, or  
4 LHRH), calcitonin, C-peptide of insulin, parathyroid hormone  
5 (PTH), human growth hormone (hGH), growth hormone (HG),  
6 growth hormone releasing hormone (GHRH), oxytocin,  
7 corticotropin releasing hormone (CRH), somatostatin analogs,  
8 gonadotropin agonist analogs (GnRHa), atrial natriuretic  
9 peptide (hANP), thyroxine releasing hormone (TRHrh),  
10 follicle stimulating hormone (FSH), or prolactin.

1 28. The method of claim 21 wherein the enhancer is  
2 a surfactant.

*Gibbs*  
1 29. The method of claim 28 wherein the enhancer is  
2 a salt of a fatty acid.

1 30. The method of claim 29 wherein the enhancer is  
2 sodium caprate.

*add  
a4*

*add  
C6*

*add H11*

*Add  
G4*

*add G6*

*Add F15*